REMARKS

I. Status of the Claims

Claims 1-6, 8-24, and 26-41 are pending in this application. Claims 7 and 25 have been canceled. Claims 30-38 have been withdrawn from consideration. Claims 1-6 and 29 stand rejected. Claim 29 has been amended as discussed below. Applicants acknowledge and appreciate the allowance of claims 8-24, 26-28 and 39-41.

Applicants acknowledge and appreciate the Examiner's withdrawal of the

1. rejection of claims 1-29 for lack of enablement under 35 U.S.C. § 112 ¶ 1;

2. rejection of claim 41 under 35 U.S.C. § 112, ¶ 2, as being indefinite;

3. rejection of claims 17-29 under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,580,857, WO 96/20703, or WO 94/26240; and

4. rejection of claims 8-29 under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as being obvious over Davis et al., *Journal of the American Podiatric Medical Association* (1989) 79:1, 24-26 ("Davis").

II. Rejection under 35 U.S.C. § 112, second paragraph

Claim 29 has been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to recite a compound of formula (I) in combination with the substances of claim 17. (*Office Action* at p. 2.)

Claim 29 refers to a method of manufacturing an anti-diabetic agent according to claim 17, which requires a combining a compound of formula (I) in combination with a substance as claimed. Thus, claim 29 has been amended to recite the compound of formula (I) "...and organic bases in combination with substances selected from the group consisting of insulin, its fragment derivatives, IGFs, and growth factors, or combinations thereof, with a pharmaceutically acceptable carrier." By this amendment,

claim 29 requires combining all of the elements of claim 17, and is thus rendered definite.

Accordingly, Applicants respectfully request withdrawal of this rejection.

III. Rejections under 35 U.S.C. §§ 102 and 103

The Examiner has maintained the rejection of claims 1-6 under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as being obvious over Davis et al., *Journal of the American Podiatric Medical Association* (1989) 79:1, 24-26 ("Davis"). (*Office Action* at p. 2.) According to the Examiner, the mice used in Davis' study allegedly had elevated blood glucose levels because they were diabetic. The Examiner contends that "administration of Gibberellins would have lowered said blood glucose levels." (*Id.* at p. 3.) The Examiner concludes that Davis' administration of Gibberellins to the mice necessarily discloses the presently claimed method. (*Id.*) Applicants respectfully traverse this rejection.

"To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.'" M.P.E.P. § 2112 (quoting *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999)). "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teaching of the applied prior art." *Id.* (quoting *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)). Applicants respectfully submit that the Examiner has failed to do so.

Claim 1 refers to a method of treating Type II diabetes and its complications and associated conditions, comprising administering a compound of formula (I). Type II diabetes is characterized by an elevated blood glucose level. (*See, e.g., Declaration of Dr. Peter Jenkins* ("the Declaration"), filed September 9, 2005, at pp. 3-4.) Example 5 demonstrates the effective treatment of Type II diabetes, attaining a normal blood glucose level, by administering Gibberellins alone. (*See Specification* at p. 22-23, *Response to Office Action* dated October 5, 2005, at pp. 24-26, and references cited therein.) As demonstrated in Example 5, treatment of Type I diabetes differs from the treatment of Type II diabetes in that treating Type I diabetes requires the adminstration of a substance such as insulin in addition to Gibberellins to attain a normal blood glucose level. (*Id.*) Indeed, allowed claim 11 is directed to the treatment of Type I diabetes with a combination of a compound of formula (I) and a substance as claimed (e.g., insulin).

In contrast to the presently claimed methods, Davis teaches a method of treating *inflammation* using a composition containing Gibberellin. (*Davis* at p. 24.) Davis used diabetic mice in its study "because of their poor healing and anti-inflammatory capabilities." (*Id.* at 24.) Davis injected a group of mice with 200 mg/kg streptozocin and then measured their blood glucose level to confirm that they had developed diabetes. (*Id.* at 24-25.) Davis then created a site of inflammation on the mice by subcutaneous injection of a 2% gelatin solution. (*Id.* at p. 25.) After administration of a Gibberellin solution, the mice were killed three hours later for analysis of inflammation activity. (*Id.*) Davis evaluated the effect of Gibberellin on inflammation by measuring

the reduction of polymorphonuclear leukocyte cells (PMNs) at the site of inflammation. (*Id.*)

While Davis does not expressly state the type of diabetes induced in its mice, one of ordinary skill in the art would readily appreciate that adminstration of such a high dose of streptozocin would have induced insulin-dependent, or Type I, diabetes. For example, Type I diabetes was induced with just 60 mg/kg streptozocin in the male Wistar rats used in Example 5. (*Declaration* at pp. 4-5.) Prior to injection with 2% gelatin to induce inflammation, Davis determined that its subject mice were diabetic, but did not report that any further blood sugar measurments were taken. (*Davis* at p. 25.) Thus, whether or not Davis' method of treating inflammation with Gibberellins necessarily discloses altering the blood glucose level of its diabetic mice must be deduced from the data available in Davis, namely the polymorphonuclear leukocyte (PMN) counts reported at various doses of Gibberellins as given in Table I. (*See Id.*)

Davis assesses the reduction of PMN cells at the inflammation site as a standard technique to measure anti-inflammatory activity. (*Id.* at p. 24.) It is well known that diabetic subjects exhibit abnormal PMN cell activity. (*See* MacRury et al., *J. Clin. Pathol.* (1989) 42:1143-1147 at 1143.) The data given in Table I on mice injected with saline instead of 2% gelatin demonstrates this abnormality. (*Davis* at p. 25.) The saline control had a PMN count of 18.1±0.7, while the saline diabetic had a PMN count of only 9.5±0.6. (*Id.*) Inducing inflammation with the 2% gelatin injection caused the saline diabetic's PMN count to increase to 28.3±0.5. (*Id.*) By adminstering increasing doses of Gibberellin, Davis observed that at a 100 mg/kg dose, the PMN count in the treated mice had decreased to 11.3±0.7. (*Id.*)

Applicants respectfully submit that Davis' increasing doses of Gibberellin brought the mice's PMN count down to a level that is substantially the same as that of the saline diabetic's beginning level, 9.5±0.6. Thus, in showing that the PMN count decreased from 28.3 to 11.3, Davis' administration of Gibberellin had treated only the 2% gelatin diabetic's inflammation because the treatment returned these mice to their initial diabetic state. Had the Gibberellin dose decreased the blood glucose level of the diabetic mice to a normal level, thereby treating their diabetes, one of ordinary skill would have predicted that the treated mice would have a PMN count similar to 18.1, that of the saline control mice which were not diabetic. Thus, the failure of Davis' Gibberellin administration to affect the diabetic state of its treated mice demonstrates that, contrary to the Examiner's allegation, blood glucose levels are not *necessarily* reduced upon treatment with Gibberellins.

In fact, Davis' inability to reduce the diabetic mice's blood glucose levels to a normal level is an expected result of its study. Davis induced diabetes with a high dose of streptozocin, such that the mice would have developed Type I diabetes. Effective treatment of Type I diabetes requires the administration of insulin or a therapeutically effective substitute. (*Declaration* at p. 3-4, 8.) In Davis' study, no insulin was administered to the diabetic mice in conjuction with the Gibberellin. Davis does not disclose, teach or suggest the use of insulin in combination with Gibberellins in treating diabetes, inflammation or any other condition. As the Examiner admits, the evidence presented in Example 5 supports the efficacy of the combination of Gibberellins and insulin for treating Type I diabetes. (*Office Action* dated October 5, 2005, at p. 3.) At

best, Davis indicates that Type I diabetes is substantially unaffected by the treatment of Gibberellins alone at the doses administered in its study.

Applicants respectfully submit that the Examiner has failed to demonstrate that Davis inherently describes the presently claimed method, and thus fails to anticipate the present claims. In addition, Davis does not teach or suggest a method of treating Type II diabetes and its complications and associated conditions, as claimed. Therefore, the Examiner has failed to establish a prima facie case of obviousness over the claimed method.

Accordingly, Applicants respectfully request withdrawal of this rejection.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 1-6 and 29 in condition for allowance. Applicants submit that the proposed amendment of claim 29 does not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Furthermore, Applicants respectfully point out that the final action by the Examiner presented some new arguments as to the application of the art against

Applicant's invention. It is respectfully submitted that the entering of the Amendment would allow the Applicants to reply to the final rejections and place the application in condition for allowance.

Finally, Applicants submit that the entry of the Amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art reference cited against this application. Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: June 30, 2006

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